

(19)



Europäisches Patentamt  
European Patent Office  
Office européen des brevets



(11)

EP 0 839 541 A2

(12)

## EUROPEAN PATENT APPLICATION

(43) Date of publication:  
**06.05.1998 Bulletin 1998/19**

(51) Int Cl. 6: **A61L 17/00**

(21) Application number: **97308688.7**

(22) Date of filing: **30.10.1997**

(84) Designated Contracting States:  
**AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC  
NL PT SE**  
Designated Extension States:  
**AL LT LV RO SI**

(30) Priority: **31.10.1996 US 741884**

(71) Applicant: **Ethicon, Inc.  
Somerville, NJ 09976 (US)**

(72) Inventors:  
• **Agarwal, Vishvaroop  
Piscataway, NJ 08854 (US)**  
• **Hunter, Alastair W.  
Bridgewater, NJ 08807 (US)**

(74) Representative: **Mercer, Christopher Paul  
Carpmaels & Ransford  
43, Bloomsbury Square  
London WC1A 2RA (GB)**

### (54) Coating mixture for surgical articles

(57) The present invention provides a coating mixture composed of a solvent selected from the group consisting of ethyl acetate, ethyl acetate/ethanol, n-propyl acetateacetone, isopropyl acetate/ethanol, ethyl acetateacetone and blends thereof; a biocompatible pol-

ymer and optionally a fatty acid salt. The present invention also provides a process for coating surgical articles comprising forming a coating mixture, contacting a surgical article with the coating mixture; and drying the coated surgical article to substantially remove the solvent.

EP 0 839 541 A2

**Description**Field of the Invention

5 This invention relates to a coating mixture for coating surgical articles such as sutures or needles and a process for coating surgical ligatures such as sutures.

Background of the Invention

10 Sutures are generally coated with a lubricious coatings to improve the tie down and knot adjustability of the suture. Additionally, these coatings may also reduce the drag associated with passing the suture through the tissue thereby reducing the tissue trauma.

15 The coatings that are applied to sutures generally contain a biocompatible low molecular weight film-forming polymer. Optionally, fatty acid salts may be added into the coating to provide further lubrication. These coatings are usually dissolved in a volatile organic solvent (such as chloroform, toluene, xylene and 1,1,2-trichloroethane) and applied to the sutures. Unfortunately, many of the volatile organic solvents used in coating sutures can pose environmental concerns. Therefore, it would be a significant contribution to the art to replace these volatile organic solvents with an environmentally benign solvent systems.

Summary of the Invention

20 We have discovered a process for coating surgical articles comprising forming a coating mixture (which includes solutions, dispersions, suspensions or emulsions) composed of a solvent selected from the group consisting of ethyl acetate, ethyl acetate/ethanol, n-propyl acetate/acetone, isopropyl acetate/ethanol, ethyl acetate/acetone and blends thereof; a biocompatible polymer and optionally a fatty acid salt; contacting a surgical articles with the coating mixture and drying the coated surgical articles to substantially remove the solvent.

25 In another embodiment of the present invention we have invented a coating mixture composed of a solvent selected from the group consisting of ethyl acetate, ethyl acetate/ethanol, n-propyl acetate/acetone, isopropyl acetate/ethanol, ethyl acetate/acetone and blends thereof; a biocompatible polymer and optionally a fatty acid salt.

Description of the Figures

30 Fig. 1 illustrates one embodiment of a coating line suitable for coating a surgical suture.

Fig. 2 illustrates a coating head which is suitable for coating a surgical suture.

35 Fig. 3 illustrates a guide means which is suitable for coating a surgical suture.

Fig. 4 illustrates one embodiment of a coating apparatus suitable for coating a surgical suture.

Detailed Description

40 Suitable solvents for use in the improved coating method are selected from the group consisting of ethyl acetate, ethyl acetate/ethanol, n-propyl acetate/acetone, isopropyl acetate/ethanol and ethyl acetate/acetone. These solvents will substantially solubilize the biocompatible polymers used in the coating mixture and may act as a liquid dispersant for other insoluble additives such as fatty acids salts.

45 Generally, the solvent will constitute from in the range of about 98 to about 80 weight percent of the coating mixture, preferably the solvent will be in the range of from 96 to 85 weight percent and most preferred in the range of from 96 to 90 weight percent (based on a total weight percent of 100 percent).

50 If the solvent system is a combination of ethyl acetate/ethanol, it should contain in the range from about 99 to about 70 weight percent ethyl acetate and preferably in the range from 90 to 80 weight percent ethyl acetate. If the solvent system is a combination of ethyl acetate/acetone, it should contain in the range from about 99 to about 1 weight percent ethyl acetate and preferably from in the range of from 90 to 10 weight percent ethyl acetate. If the solvent system is a combination of n-propyl acetate/acetone, it should contain in the range from about 90 to about 25 weight percent n-propyl acetate and preferably in the range from 80 to 40 weight percent n-propyl acetate. If the solvent system is a combination of isopropyl acetate/acetone, it should contain in the range from about 65 to about 10 weight percent isopropyl acetate and preferably about 55 to about 10 weight percent isopropyl acetate. The weight percent of the solvent is based on the total weight percent of the solvents totaling 100 percent.

55 Suitable biocompatible polymers useful in the coating mixture include homopolymers and copolymers (including random copolymers and block copolymers, which for the purpose of this application shall include any polymer containing two or more repeating units unless otherwise limited) of lactide(which includes L-, D- and meso-lactides and combi-

nations thereof unless otherwise specified), glycolide,  $\epsilon$ -caprolactone, p-dioxanone, trimethylene carbonate, alkyl substituted derivatives thereof and combinations thereof (such as polylactide, polyglycolide, and copolymers of lactide and glycolide with each other and with other lactone type monomers such as  $\epsilon$ -caprolactone, p-dioxanone, trimethylene carbonate and methyl substituted derivatives thereof), poly(alkylene oxalate), copolymers of vinyl acetates with unsaturated carboxylic acids (such as crotonic, acrylic, and methacrylic acids), water soluble or dispersible cellulose derivatives (such as methyl cellulose, hydroxymethyl cellulose and carboxymethyl cellulose); natural gums; ethylene oxide polymers polyacrylamide; collagen; gelatin; polyamino acids; polyvinyl alcohol; absorbable conjugated unsaturated triglycerides such as dehydrated castor oil, and mixtures of such polymers. Particularly preferred are film-forming polymers and copolymers, including but not limited to copolymers of L-lactide and glycolide which contain from about 5 15 to 85 percent L-lactide, and have an inherent viscosity of from about 0.5 to 2.0 measured as a 0.1 percent solution in hexafluorisopropanol at 25°C.

The fatty acid salts useful in the coating compositions of the present invention are biocompatible salts of fatty acids including the calcium, magnesium, barium, aluminum, and zinc salts of six carbon and higher fatty acids, particularly those having from about 12 to 22 carbon atoms and mixtures thereof. The calcium salts of stearic, palmitic and oleic acids are particularly preferred for use in the present invention.

The ratio of the biocompatible polymer and the fatty acid salt in the coating composition may vary depending upon the specific components selected and the particular suture being coated. In general, the preferred ratio of polymer to salt is within the range of 2:1 to 1:2 by weight, although useful compositions are obtained over a wider range of from about 1:4 to 4:1 parts by weight.

The coating mixture may be applied as a coating using conventional techniques. For example, the surgical articles can be immersed in the coating suspension to coat its surface. Once the surface is coated, the surgical article can be removed from the mixture where it can be dried at an elevated temperature until the solvent and any residual reactants are removed.

Although it is contemplated that numerous surgical articles (including but not limited to endoscopic instruments) 20 can be coated with the coating mixture of this invention to improve the surface properties of the article, the preferred surgical articles are surgical sutures and needles. The most preferred surgical article is a suture, most preferably attached to a needle.

Sutures coated with the polymers of this invention are desirable because they have a more slippery feel, thus making it easier for the surgeon to slide a knot down the suture to the site of surgical trauma. In addition, the suture is 30 more pliable, and therefore is easier for the surgeon to manipulate during use. These advantages are exhibited in comparison to sutures which do not have their surfaces coated with the polymer of this invention.

With surgical articles (such as sutures) composed of homopolymers or copolymers of lactide and glycolide, the biocompatible polymers in the coating composition is preferably polylactide or a copolymer of L-lactide and glycolide containing at least about 15 percent L-lactide, and preferably having different solubility characteristics than the suture.

35 For example, a suture made of a lactide-glycolide copolymer containing about 10 percent of lactyl moieties may be coated with a composition containing, as a biocompatible polymer, a lactide-glycolide copolymer containing about 65 percent of lactyl moieties, which copolymer is more readily soluble in the inventive solvent system than the suture material.

The biocompatible polymer in the coating composition may, if desired, be the same composition as the surgical 40 article provided that precautions are taken to avoid dissolving the suture when the coating composition is applied. This can be done by utilizing a coating composition in which the biocompatible polymer is in mixture at substantially saturation levels and the contact time of the surgical article with the coating composition is short before the solvent is driven off.

Where the compositions of the surgical article and the biocompatible polymers are identical, and in other instances 45 where the surgical article may be subject to some surface dissolution and/or surface swelling or softening by reason of the action of the solvent thereon, there may be a gradual transition between the substrate composition and the coating composition rather than a sharp interface between them. There may also be some weakening of the surgical article accompanying the application of such coating compositions.

The coating composition may, if desired, also contain components other than those discussed above for other 50 useful purposes including dyes, antibiotics, antiseptics, anesthetics and anti-inflammatory agents.

The amount of coating composition applied to the surgical article, or the coating add-on, will vary depending upon the surgical article and the purpose of the coating. For sutures the construction of the fiber, e.g., the number of filaments and tightness of braid or twist will be important parameters in determining the amount of coating add-on. In general, the coating composition applied to a braid will constitute from about 0.1 to about 10 percent by weight of the coated 55 fiber, but coating composition may range from as little as about 2 percent by weight to as much as about 15 percent or higher in some cases. As a practical matter, and for reasons of economy and general performance, for suture coatings it is generally preferred to apply the minimum amount of coating composition consistent with good tie-down performance, and this level of coating is readily determined experimentally for any particular fiber-coating system.

The coatings are applied to any suture material where it is desired to improve fiber lubricity, suture tie-down characteristics, or the like. The coating is particularly useful with synthetic absorbable multifilament sutures such as homopolymers and copolymers of glycolide, lactide (which includes L-, D-, and meso- forms of lactide and mixtures thereof),  $\epsilon$ -caprolactone, p-dioxanone, trimethylene carbonate, 1,4-dioxepan-2-one, poly(alkylene oxalate), and mixtures of such polymers with each other and with other compatible absorbable compositions as those described; for example, in U.S. Pat. Nos. 3,636,952 and 2,683,136 which patents are herewith incorporated herein by reference. One suitable suture composition would include copolymers of p-dioxanone, trimethylene carbonate and glycolide and copolymers of lactide and p-dioxanone. Preferred are suture compositions derived from lactide and glycolide sometimes referred to herein as simply homopolymers and copolymers of lactide and glycolide and copolymers of glycolide and  $\epsilon$ -caprolactone.

It will be readily appreciated that the coating may likewise be used with good results on absorbable monofilament sutures as well as on nonabsorbable monofilament and multifilament sutures.

Nonabsorbable sutures such as cotton, linen, silk, nylon, polyethylene terephthalate and polyolefins are normally coated with nonabsorbable compositions. Polyolefins are usually of monofilament construction while cotton, linens, silk and polyester are usually of braided, twisted or covered multifilament construction. While there is usually no requirement that the coating on such sutures be absorbable, the coating composition may, nevertheless be used as a lubricating coating for nonabsorbable sutures if desired.

The coating mixture usually is applied to the final suture structure in order to provide a substantially continuous coating on at least the outward facing surfaces of the outer-most filaments of the braid. It is understood, however, that the coating mixture may be applied, if desired, to the individual filaments before they are formed into strands or to the individual strands before they are formed into the final suture structure. This invention is not limited as to suture size or composition, but may be practiced, for example, with sutures from size 9-0 to size 2 and larger, and with other suture materials. In coating multifilament sutures with the coating mixture of this invention, it is not necessary that every filament within the suture be individually or completely coated.

The improvement in tie-down properties imparted to synthetic absorbable sutures may be determined semi-quantitatively by comparing the feel of coated and uncoated sutures during the act of tying down a single throw knot. Such comparisons are preferably made on both wet and dry sutures since many suture materials have different tie-down properties when tested wet or dry.

Sutures may be coated using a variety of coating systems. One suitable system for coating sutures is illustrated in Figures 1-4. As shown in Figure 1 a spool 2 of suture 4 is placed on let off device 6. The suture 4 travels from let off device 6 to the coating head 20 as shown in Fig. 2. The coating head 20 comprises a support 22 to which are attached a first guide means 30 and second guide means 32 (which as illustrated comprise guide rollers but may include wire loops or pigtails) for directing the suture 4 into the coating mixture 25 contained in vessel 24 and preferably secured in position relative to said vessel 24. The guide rollers are made of a nontoxic nonreactive material which is inert to the solvents employed in the coating mixture. Preferably the guides rollers will be coated with a nonreactive material such as a ceramic, or stainless steel alloy (such as the rollers manufactured by Yuasa of Japan). The first guide means 30 redirect the suture 4 from a horizontal path to a path which is substantially vertical and downward. The first guide means 30 may be associated with one or more additional guide means (as illustrated in Figure 2 guide roller 28) which reorients the suture to a substantially vertical path. The suture 4 then travels from the first guides means 30 to a second guide means 32 which orients the suture 4 to a substantially vertical path which is upward (which is preferably perpendicular to the surface of the coating mixture). The second guide means 32 may be associated with a third guide means 34. The third guide means 34 may be associated with one or more auxiliary guide means to further reorient the suture such as guide means 36 and 38.

As the suture passes from the guide roller 30 to guide roller 32 it is submerged in coating mixture 25 and is coated with the coating mixture 25 to provide a wet coated suture 5. After the wet coated suture 5 has been reoriented by the guide roller 32 it emerges from the coating mixture 25 as a wet coated suture 5 and is turned through a sharp turn which is designed to generate sufficient centrifugal force to remove the excess coating mixture entrained with the suture. The angle of the turn will vary depending on the composition and density of the coating mixture, the speed that the suture is moving, the viscosity of the coating mixture and the size of the suture. Currently it is preferably for sizes 0 to 8-0 suture that the turn be at least about 120 degree turn by guide means 34 and preferably through at least about 160 degree turn suture (using the preferred calcium stearate, film-forming polymer mixture in ethyl acetate).

Alternatively, the excess coating may be removed from the surface of the suture after it emerges from contacting the coating by positioning a surface in close proximity (adjacent) to the path of the suture or in contact with the suture as it exits the vessel. The surface should be placed close enough to the surface of the suture to form a meniscus with the wet coated suture. The meniscus will facilitate the removal of the excess coating mixture and may have various geometries from a rounded point to a flat surface. In one embodiment of the invention it is proposed to size the guide means 34 with the sides of the guide means 34A and 34B being suitable for forming a meniscus 300 and removing the excess coating mixture as shown in Fig. 3.

Guide means 34 is important for separating the excess coating mixture from the wet coated suture 5, which substantially prevents an uneven coatings from being deposited on the suture. Guide means 34 reorients the coated suture 5 from a vertical upward path to a path that is substantially vertical and downward. From guide roller 34 the coated suture 5 travels to guide roller 36 which reorients the coated suture 5 into a substantially horizontal path. The coated suture 5 then optionally travels to guide roller 38 which completes the orientation of the coated suture 5 to a substantially horizontal path.

In an another embodiment of the invention when the coated suture 5 emerges from the coating mixture 25, excess coating mixture 25 is entrained with the wet coated suture 5. The excess coating mixture falls off the coated suture 5 as it travels through guide means 34 (as shown in Fig. 2). As the excess mixture drips off the coated suture 5, it is caught by a diverter 40 which partially or completely prevents it from returning to the coating mixture 25 and changing the concentration of the coating mixture 25. Maintaining a substantially constant concentration of solvent to the biocompatible polymer and optionally fatty acid is important to maintaining a uniform suture coating. The coating mixture caught by the diverter 40 may be fed to a reservoir for reconstitution and reuse or disposed of. The diverter 40 significantly improves the final suture product by insuring a uniformly coated suture is produced throughout the coating process. The diverter 40 can constitute a plate that completely separates the vessel into an upper and lower section.

Alternatively, some of the coating mixture may be returned to the coating bath to minimize waste. However, the amount returned to coating bath must not be enough to adversely affect the concentration of the coating bath. The drip guard 440 shown in Figure 4 provides a means for returning some of the excess coating mixture to the coating bath. The drip guard 440 as shown in Fig. 4 has two side members 442 and 444 attached along opposite sides of base 446. The excess coating mixture coming off of the suture at guide means 34 is directed by the drip guard 440 into the diverter. Suture lines without drip guard 440 drip the excess coating mixture directly into the vessel through the same opening in the diverter that provides access to guide means 32. The excess coating mixture not returned to the vessel is directed by diverter plate 450 to drain 452.

Additionally, the guide roller assembly shown in Fig. 2 and Fig. 4 allows sutures to be coated at processing speed of greater than 175 feet per minute and will preferably operate in the range of from about 200 to about 450 feet per minute.

The level of the coating mixture 25 in the vessel 24 is maintained at a constant level and additional coating mixture 25 is supplied by coating reservoir 26 which is in fluid communication with vessel 24 by means of an outlet in the reservoir, a conduit 456 and an inlet 454 in the vessel (as shown in Fig. 4). The vessel 24 and reservoir 26 may be equipped with a temperature controlling means, recirculating means and/or an agitating means to assure the coating mixture remains uniform (such as the magnetic stirring bar 37 shown in vessel 24). The coating mixture level in the vessel 24 may be maintained at a constant level by an automatic feed system which controls the transfer of coating mixture from the reservoir 26 to the vessel 24. A gravity feed system or mechanical system may be used for this purpose. The vessel 24 during operation may be closed or covered with a cover 23 to prevent the solvent in the coating mixture from volatilizing into the air. The cover may also be connected to a vent assembly 41 to remove solvent vapors from the work area. Alternately, the coating assembly may be enclosed in a hood or placed in close proximity to a fume remove vent.

After the wet coated suture 5 leaves the coating head 20, it proceeds to a drying tunnel 44 where the coating mixture is dried on the coated suture 5 and the solvent is substantially removed. The drying tunnel 44 should be maintained at a temperature of from about 20°C to about 125°C, preferably in the range of from about 40°C to about 65°C and most preferably in the range of from about 45°C to 55°C. The drying tunnel 44 should also have a gas flow (filtered air or inert gas such as nitrogen, carbon dioxide etc. with a moisture content preferably of less than 30 percent) throughout the tunnel (preferably in the opposite direction of coated suture 5) in an amount sufficient to provide the desired degree of drying in a desired amount of time. Generally the air flow will be in the range of about 25 to about 3000 cu.ft./min., preferably in the range of from about 50 to about 800 cu.ft./min. and most preferably 55 to 75 cu.ft./min. The coated suture 5 will have a residence time in the drying tunnel 44 sufficient to render the suture dry to the touch and remove substantially all the coating mixture solvent. Currently, it is preferred for the coated sutures to reside in the drying tunnel 44 or from about 1 to about 20 seconds and most preferably for from about 3 to about 7 seconds. The amount of time the coated suture 5 is in the drying tunnel can be increased by adding two turning guide such as guide rollers 46 and 48 in the drying tunnel 44 to the allow the suture to traverse the tunnel several times.

The dried suture may then be taken up on a take up spool 64, preferably the suture will first travel through a godet drive 60 to equilibrate the tension on the coated suture 5 and then it will travel to a take up winder 62.

Those skilled in the art will also appreciate that by placing additional spools on the let off device 6 and a plurality of guide means in parallel on frame 22, that several sutures could be simultaneously coated by a single coating head 20. The presence of additional sutures would also require adjustments in the air flow and a take up winder 62 capable of winding multiple spools of sutures. It is currently preferred to coat one to six sutures simultaneously.

The following non-limiting examples are provided to further illustrate the present invention.

Example 1

This example describes the solubilities of a 65/35 polylactide-polyglycolide copolymer and calcium stearate coating in various solvents. The 8 weight percent of coating was mixed with 92 weight percent of each of the solvent systems described in Table 1. The mixing was performed at ambient temperature.

<b>Solvent/Blend with 8% w/w copolymer</b>	<b>Solubility with 65/35 copolymer</b>
92% w/w ethyl acetate 8% w/w copolymer	Clear
92% w/w (85% ethyl acetate + 15% ethanol)	Clear
92% w/w (n-propyl acetate	Partial
92% w/w (75% n-propyl acetate + 25% acetone)	Clear
92% w/w (50% n-propyl acetate + 50% acetone)	Clear
92% w/w (50% n-propyl acetate + 50% ethanol)	Insoluble
92% w/w isopropyl acetate	Partial
92% w/w (85% w/w isopropyl acetate + 15% ethanol)	Partial
92% w/w (75% w/w isopropyl acetate + 25% acetone)	Partial
92% w/w (50% w/w isopropyl acetate + 50% acetone)	Clear
92% w/w (50% ethyl acetate + 50% acetone)	Clear

The formation of a clear solution indicated that the coating was soluble in the solvent. The formation of a cloudy mixture indicated that the coating was partially soluble in the solvent. The coating failed to dissolve into the 50% n-propyl acetate and 50% ethanol solution.

**Claims****1. A process for coating surgical articles comprising**

35 forming a coating mixture composed of a solvent selected from the group consisting of ethyl acetate, ethyl acetate/ethanol, n-propyl acetate/acetone, isopropyl acetate/ethanol, ethyl acetate/acetone and blends thereof; a biocompatible polymer and optionally a fatty acid salt;

contacting a surgical article with said coating mixture to provide a wet coated surgical device; and

40 drying the wet coated surgical article to substantially remove the solvent to provide a coated surgical article.

**2. The process of claim 1 wherein the biocompatible polymer is selected from the group consisting of homopolymers and copolymers of lactide, glycolide,  $\epsilon$ -caprolactone, p-dioxanone, trimethylene carbonate, alkyl substituted derivatives thereof, poly(alkylene oxalate), copolymers of vinyl acetates with unsaturated carboxylic acids, water soluble or dispersible cellulose derivatives, natural gums, ethylene oxide polymers, polyacrylamide, collagen, gelatin, polyamino acids, polyvinyl alcohol, absorbable conjugated unsaturated triglycerides and combinations and mixtures thereof.****3. The process of claim 1 or claim 2 wherein the Fatty acid salt has from 12-22 carbon atoms.****4. A coating mixture comprising a solvent selected from the group consisting of ethyl acetate, ethyl acetate/ethanol, n-propyl acetate/acetone, isopropyl acetate/ethanol, ethyl acetate/acetone and blends thereof; a biocompatible polymer selected from the group consisting of homopolymers and copolymers of lactide, glycolide,  $\epsilon$ -caprolactone, p-dioxanone, trimethylene carbonate, alkyl substituted derivatives thereof, poly(alkylene oxalate), copolymers of vinyl acetates with unsaturated carboxylic acids, water soluble or dispersible cellulose derivatives, natural gums, ethylene oxide polymers, polyacrylamide, collagen, gelatin, polyamino acids, polyvinyl alcohol, absorbable conjugated unsaturated triglycerides and combinations and mixtures thereof and a fatty acid salt having from 12-22**

carbon atoms.

5. The coating mixture of claim 11 wherein polymer is selected from the group consisting of homopolymers and copolymers of lactide, glycolide,  $\epsilon$ -caprolactone, p-dioxanone, trimethylene carbonate, alkyl substituted derivates thereof and combinations thereof.
6. The coating mixture of claim 4 wherein the fatty acid salt is selected from the group consisting of biocompatible salts of stearic, palmitic and oleic acids.
- 10 7. The coating mixture of claim 4 wherein the solvent is ethyl acetate/ethanol containing in the range from about 90 to about 80 weight percent ethyl acetate.
8. The coating mixture of claim 4 wherein the solvent is ethyl acetate/acetone containing in the range from about 90 to about 10 weight percent ethyl acetate.
- 15 9. The coating mixture of claim 4 wherein the solvent is n-propyl acetate/acetone containing in the range from about 80 to about 40 weight percent n-propyl acetate.
- 20 10. The coating mixture of claim 4 wherein the solvent is isopropyl acetate/acetone containing in the range from about 55 to about 10 weight percent isopropyl acetate.

25

30

35

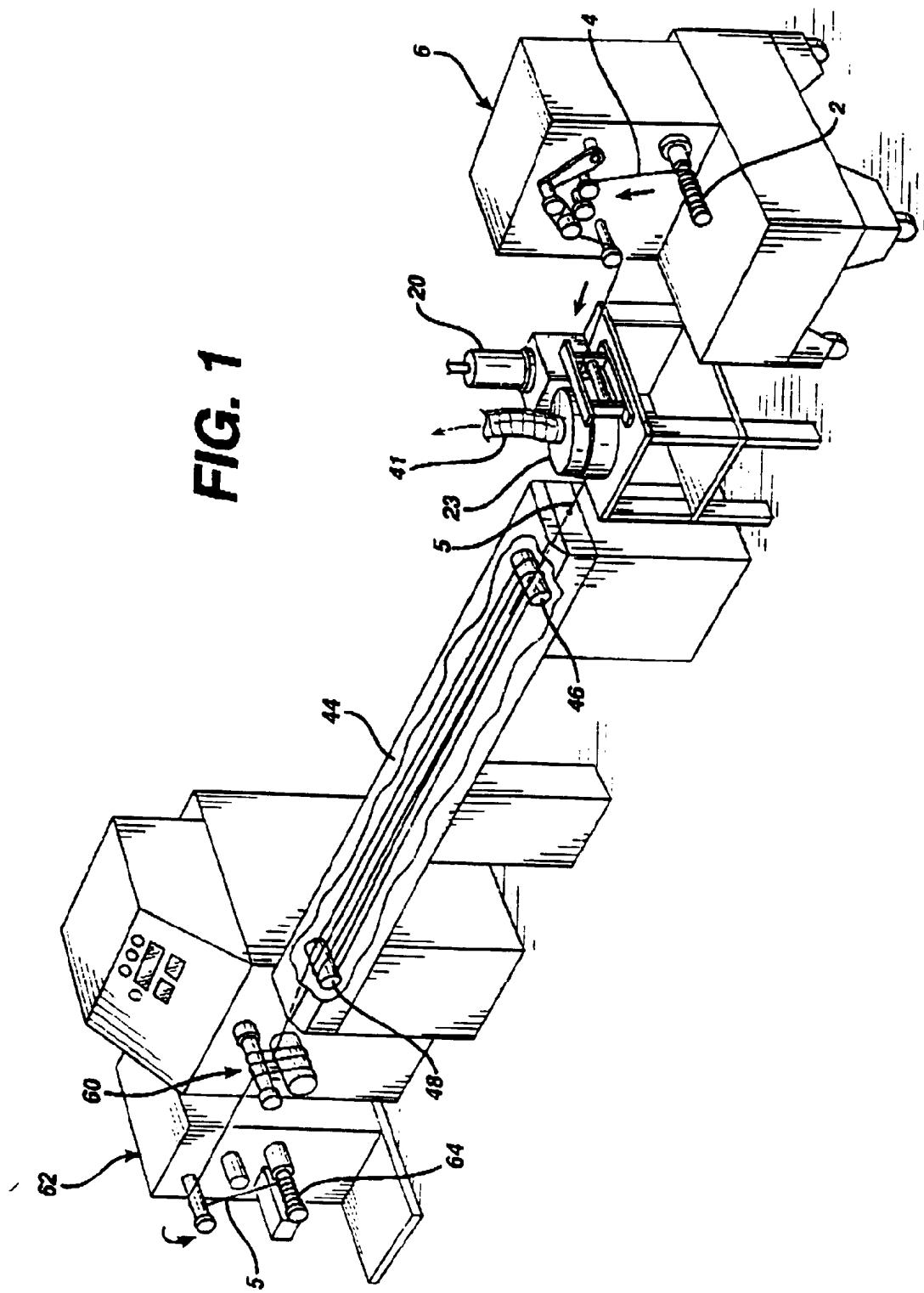
40

45

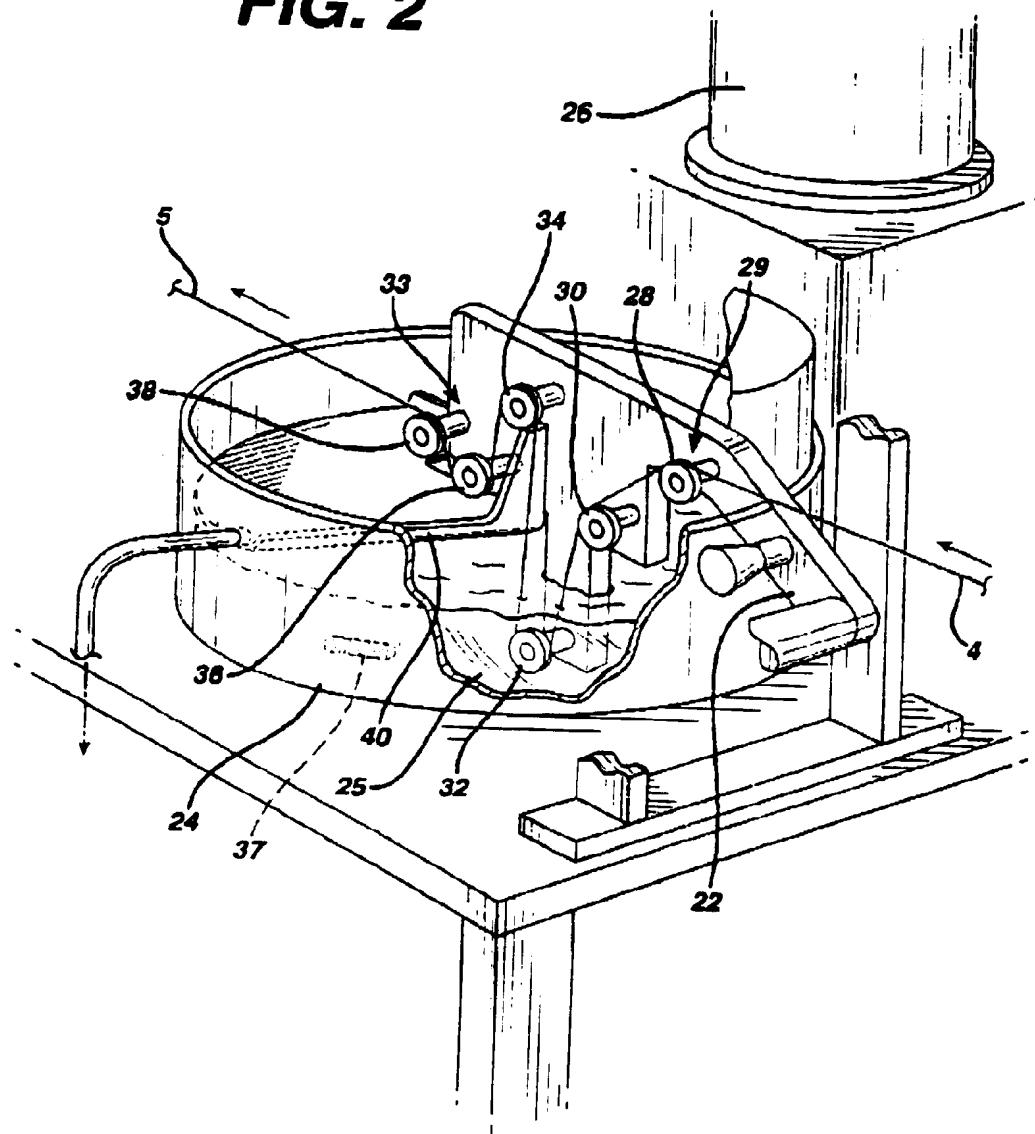
50

55

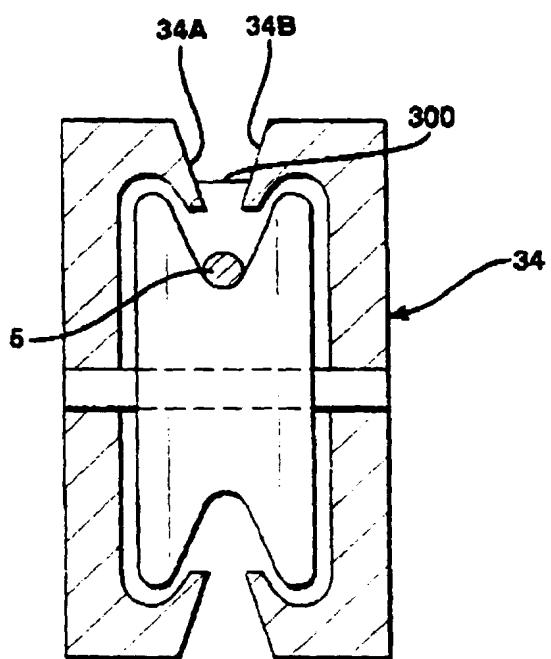
**FIG. 1**



**FIG. 2**



**FIG. 3**



**FIG. 4**

